containing the proteins in discrete areas of an array that physically separate the at least two samples,

providing a plurality of antibodies wherein each member of the plurality of antibodies is identified as having specific binding affinity to an expression product of a gene sequence,

contacting each of the at least two samples with the member of the plurality of antibodies at the discrete areas of the array,

detecting an antibody-binding reaction between the member of the plurality of antibodies and the proteins contained at the discrete areas of the array, and

identifying differential gene expression between the at least two distinct biological conditions by correlating differences in the antibody binding reaction in the at least two samples with expression of the gene sequence identified with the member of the plurality of antibodies.

15. (New) The method of claim 1 wherein the step of providing a plurality of antibodies is comprised of obtaining *in vivo* expression of the gene sequence to yield murine polyclonal antibodies having specific binding affinity to the expression product of the gene sequence.

16. (New) The method of claim 14 wherein the step of contacting the at least two samples with the member of the plurality of antibodies is comprised performed on at least 100 samples.

17. (New) The method of claim 14 wherein the step of providing at least two samples that exhibit differential gene expression is comprised of providing a first sample comprised of

protein extract from normal human tissue and a second sample comprised of protein extract from a diseased sample of the same tissue.

18. (New) The method of claim 17 wherein the second sample is protein extract from cancer cells or tissue.

19. (New) The method of claim 17 wherein the diseased sample results from exposure to a chemical agent.

20. (New) The method of claim 18 wherein the identifying step is comprised of identifying genes that are differentially expressed in cancerous tissue.

21. (New) The method of claim 14 further comprising the step of identifying the expression product of the gene sequence.

22. (New) The method of claim 14 further comprising the step of raising a monoclonal antibody to the expression product of the gene sequence.

23. (New) The method of claim 14 further comprising the step of determining the polynucleotide sequence of the gene sequence.

Resolution of Issues of Claim Terminology Under 35 USC § 112 Address in Previous Action

Referring to the paragraphs of the Office Action in the previously pending application, at paragraph 12, the Examiner objects to use of the terms "a plurality of samples of biological material comprising a polypeptide..." This language refers to the portion of the invention described in the independent claim wherein the samples are placed in an array for analysis such that the proteins can be contacted with the antibodies as is described in the remainder of the claim. In the new claims, the corresponding step specifies that the samples comprise human proteins. This language is derived directly from the description of the invention and the working examples in the present specification and clearly satisfies the written description requirement of 35 USC § 112, 1st paragraph.

Regarding the previous claim 3, new claim 16 clarifies that at least 100 different samples are analyzed. A written description for this step clearly exists at pages 11-13 of the specification and in the accompanying figures.

Iris et al. Does Not Disclose a Reaction Between an Antibody and a Human Protein Where the Antibody Protein Reaction Identifies the Differentially Expressed Gene as in Claim 1 of the Present Invention.

Iris et al. present a technology to screen nucleic acid mutations for polymorphisms and only performs gene expression analysis using oligonucleotide probes to RNA, with labels such as peptide tags, that are captured on addressable antibody arrays for analysis by fluorescence photometry. The main focus of Iris et al. is detection of single nucleotide polymorphisms (SNPs).

In Iris et al., the antibodies are attached to solid phase and are immunospecific to peptide labels that are attached to oligonucleotide probes. The peptides are not proteins from human tissues. These probes hybridize with SNPs in a sample containing nucleic acids. There is no reaction between an antibody that is specific for the expression product of a gene and a protein present in the patient sample such that differentially expressed genes are identified.

The cited portions of Iris et al. related to analysis of gene expression (Section 5.3, columns 14-15) detect a signal indicating the presence of an aberrantly spliced target RNA even where the mutation of the aberrant splice is silent in the resulting protein (See Iris et al., column 15, lines 1-24). Thus, Iris et al. clearly do not depend on a specific antibody protein reaction to differentiate gene expression in the sample. As indicated in claim 1, the present invention is different because it detects differential gene expression based on the presence of differentially expressed proteins present in tissues from different biological conditions.

Furthermore, in Iris et al., the solid phase comprises a plurality of loci, wherein each locus comprises an antibody specific to one or more of the peptide labels of oligonucleotide probes. In contrast, the method claimed in the present invention isolates and physically separates different samples to be contacted with one given antibody, i.e., the member of the plurality of antibodies as claimed, which is an antibody against a known or unknown polypeptide expressed by an identified gene sequence. In the claimed invention, the antibody-protein binding reaction identifies the gene sequence because each antibody identifies a gene sequence. Not so with Iris et al., where the method requires nucleic acid hybridization to distinguish the SNP.

In the pending claims, the differential binding reaction between the at least two samples enables the differential gene expression profiling between two distinct biological conditions.

In Iris et al., the binding reaction only fixes a labeled probe, no information is conveyed by the reaction. In the present invention, the antibody-protein reaction actually identifies the differential gene sequences expressed. This element is explicitly recited in the new claims and is nowhere found in Iris et al.

With regard to the Examiner's other comments, these are not product-by-process claims. The pending claims recite method steps that define novelty. No claim to novelty of specific antibody products per se is made as a result of practicing the recited method. The method step of in vivo expression maybe one part of a complete method that is, in toto, novel, but the product-by-process doctrines do not apply.

In light of the above, applicant requests favorable consideration and allowance of all of the newly presented claims. If the Examiner has any questions regarding the foregoing, or if the Examiner believes that an interview would facilitate the examination of this application, or if any additional information is required, the Examiner is invited to contact the undersigned at 949/567-6700, X 7740.

Respectfully submitted,

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